

AD_____

Award Number: W81XWH-04-1-0448

TITLE: Dietary Fat, Eicosanoids and Breast Cancer Risk

PRINCIPAL INVESTIGATOR: Susan K. Raatz, Ph.D.

CONTRACTING ORGANIZATION: University of Minnesota
Minneapolis, Minnesota 55455

REPORT DATE: April 2005

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

20050819144

REPORT DOCUMENTATION PAGEForm Approved
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE April 2005	3. REPORT TYPE AND DATES COVERED Annual (1 Apr 2004 - 31 Mar 2005)	
4. TITLE AND SUBTITLE Dietary Fat, Eicosanoids and Breast Cancer Risk			5. FUNDING NUMBERS W81XWH-04-1-0448	
6. AUTHOR(S) Susan K. Raatz, Ph.D.				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of Minnesota Minneapolis, Minnesota 55455 E-Mail: raatz@med.umn.edu			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited				12b. DISTRIBUTION CODE
13. ABSTRACT (Maximum 200 Words) Epidemiological and animal studies associate high levels of dietary fat with increased risk of sex hormone mediated cancer, such as breast cancer. A high intake of total fat and omega-6 fatty acids increases risk while omega-3 (n3) fatty acids are associated with risk reduction. Our proposal is testing the effect of dietary fat and fatty acids on sex hormone concentrations in post-menopausal women. The objectives are to evaluate 1) the effects of total fat and n3 intake on plasma and urinary sex hormone levels, 2) the relationship between plasma fatty acids and plasma and urinary sex hormones, and 3) the effects of total fat and n3 on the association between sex hormone concentrations and urinary prostaglandin E ₂ (PGE ₂). We are performing a randomized, Latin square-designed controlled feeding study testing High Fat, Low Fat, and Low Fat + n3 diets, each of 8 week duration. In order to determine the estrogenic effects of the diets, sex hormone endpoints will be measured reflecting availability, metabolism, and action. Plasma fatty acids fractions and urinary PGE ₂ will be measured to evaluate mechanistic effects. At present 14 women have been screened and 5 are currently enrolled in the trial. No data has yet been generated.				
14. SUBJECT TERMS Dietary fat, omega-3 fatty acids, eiconsanoids, sex hormones				15. NUMBER OF PAGES 16
				16. PRICE CODE
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

Table of Contents

Cover.....	1
SF 298.....	2
Introduction.....	4
Body.....	4
Key Research Accomplishments.....	5
Reportable Outcomes.....	5
Conclusions.....	5
References.....	5
Appendices.....	6

Introduction

Our project addresses important questions about the effects of dietary total fat and fatty acids on sex hormone concentrations in postmenopausal women. The study is being conducted at the General Clinical Research Center of the University of Minnesota. Our guiding hypothesis is that dietary total fat and fatty acid content affect sex hormone concentrations in a manner associated with sex hormone mediated cancer risk. The specific objectives are 1) to evaluate the effects of total fat and omega-3 fatty acid intake on plasma and urinary sex hormone levels in postmenopausal women, 2) to evaluate the relationship between plasma concentrations of specific fatty acids and concentrations of plasma and urinary sex hormones, and 3) to evaluate the effects of total fat and omega-3 fatty acids on the association between sex hormone concentrations and urinary prostaglandin E₂ and thromboxane B₂ concentrations.

We are conducting a well controlled feeding study to evaluate the role of fat and fatty acids in 24 healthy, postmenopausal women. The diets being tested include a "high risk" American diet (40% fat), a low fat diet (20% fat) and a low fat diet with supplemental omega-3 fatty acids (23% fat). Endpoints are being measured to assess availability, metabolism, and action of sex hormones in response to the diets. Plasma fatty acids fractions and urinary prostaglandin E₂ is being measured to evaluate mechanistic effects of dietary fat.

Increased understanding of the mechanisms by which dietary fat affect sex hormone action may provide critical information for the development of cancer-preventative dietary recommendations. Nutrition information provided as focused guidelines regarding fat intake can be developed for public use that indicate which types of foods to include in the daily diet and which to avoid.

Body

Study Progress:

The project is proceeding along the time line as defined in our statement of work. Although notification of recommendation for funding was received

Final approval for initiation of the project was received from the Donna S. Ferrandino, PhD, Human Subjects Protection Scientist on 10/15/2004 to submit our revised consent form to the local (University of Minnesota) IRB for approval. Final approval to initiate the project was then received from the University of Minnesota Human Subject Protection Program/Internal Review Board on 10/29/2004.

In order to meet final approval, the development of the diets for the intervention and nutrient calculations of the test diets were completes. Once final approval was secured, work was initiated to develop the food production procedures and coordinate the study needs within the General Clinical Research Center at the University of Minnesota.

Extensive recruitment efforts were initiated as soon as final approval was obtained. We have advertised by placing fliers throughout the medical campus and surrounding campus buildings. A text ad was placed in the Fairview University Medical Center staff and patient flier. To date 14 subjects have been screened by telephone, 6 subjects have been screened at the research

center and 5 subjects are currently participating in the feeding trial. Due to the large time commitment of the trial, careful screening is performed to reduce the possibility of drop-outs from the trial.

Presently no data are available for evaluation. It is our intention to analyze the samples in batches of 4 subjects as they complete the feeding trial. Completion of the feeding phase of the study will take 40 weeks (3-8 week diets with 2-8 week wash-out periods between diets).

Personnel:

The following personnel are presently supported on this grant

Susan Raatz PhD RD, Principle Investigator (5% effort)

Mindy Kurzer PhD, Co-investigator (5% effort)

J Bruce Redmon MD, Co-investigator (5% effort)

Michael Walcher, Senior Scientist (25% effort)

Krista Lundquist, Student Food Service Worker (50% effort)

Shanna Miller, Student Food Service Worker (25% effort)

Key Research Accomplishments

Presently no data are available for evaluation. It is our intention to analyze the samples in batches of 4 subjects as they complete the feeding trial. Completion of the feeding phase of the study will take 40 weeks (3-8 week diets with 2-8 week wash-out periods between diets).

Reportable Outcomes

Training:

This project was included as a rotation project for the Minnesota Consortium for Complementary and Alternative Medicine (CAM) Clinical Research predoctoral Summer Internship from May through August 2004, Michael Croy, RD MS, a graduate student in Human Nutrition worked on the developmental phase of the dietary component of the study.

Lindsay Orr, BA is the current Graduate Research Assistant working on the project. She is a doctoral student in Human Nutrition and is currently funded from a University of Minnesota Graduate School Fellowship. She will be funded by this project in the fall. Lindsay has been performing coordination duties for this trial.

Conclusions

The study is progressing as projected on the "Statement of Work". Given the nature of a long term feeding trial, no reportable data has yet been obtained. The study progress is as expected with recruitment of participants proceeding smoothly. The test diets are well accepted by the participants, all endpoint visits have gone well. We anticipate completion of the first wave of 5 subjects by the fall.

References

None

Appendices

Appendix 1: Diets for Intervention (Statement of Work Task 1)

Sample Menu 2000 Kcal - Day 1

Menu	High Fat	Low Fat	Low Fat + Omega 3
Breakfast			
Grapefruit Juice	130g	200 g	200 g
Cheerios	40g	32g	35g
w/ Sugar	0g	6g	6g
Bran Muffin	75g (High Fat)	60g (Low Fat)	60g (Low Fat)
w/ Butter	10g	4g	4g
Skim Milk	240g	250g	230g
Lunch:			
Turkey Sandwich			
Whole Wheat Bread	60g	60g	60g
Turkey Breast	70g	55g	45g
Butter	6g	0	5g
Mayonnaise, Regular	10g	6g	0g
Miracle Whip	0	10g (Fat Free)	10g (Fat Free)
Egg yolk	2g	5g	4 g
Flax oil	0g	0	3g
Lettuce	20 g	20 g	20 g
Tomato	50 g	50 g	50 g
Pretzels	0	25g	0
Potato Chips	35g	0	0
Applesauce	140g	180g	200g
Dinner:			
Orange Roughy	140g	90g	0
Baked Salmon	0	0	75g
w/Cajun Spice/Lemon Juice	Dash/5g	Dash/5g	Dash/5g
White Rice	140g	110g	110g
Broccoli	80g	80g	80g
Lettuce/Carrot Salad	50g/15g	50g/15g	50g/15g
Fat Free French Dressing	15g	20g	15g
w/Corn Oil	7g	5g	0
w/Flax Oil	0	0	5g
Whole Wheat Bread	26g	40g	40g
w/Butter	6g	6g	0
Angel Food Cake	0	50g	50g
w/Strawberries/Sugar	120g/0	120g/6g	120g/6g
Snack			
Wheat Thins	10g	20g (Regular)	30g (Reduced Fat)
Mozzarella Cheese	0	30g	40g
Cheddar Cheese	20g	0	0
Gumdrops	0	30g	15g
Grape Juice	0	120g	0
Nutrient Composition (Calculated)			
Kcal	2020	2011	2015
CHO (g/%)	233g/45%	329g/65%	317g/62%
Pro (g/%)	77g/15%	76g/15%	77g/15%

Fat (g/%)	92g/40%	46g/20%	54g/23%
Fiber (g)	22.8g	23.9g	25.2g
Chol (mg)	209mg	203mg	210mg
SFA (g)	28.2g	13.4g	14.8g
MUFA (g)	28.7g	13.9g	16.2g
PUFA (g)	28.0g	13.3g	16.1g
18:3 (g)	1.40g	0.85g	5.36g
20:5 (g)	0g	0g	0.46g
22:6 (g)	0.03g	.03g	0.99g
Omega 3 FA (g)	1.43g	0.88g	6.82g

Sample Menu 2000 Kcal) - Day 2

<i>Menu</i>	<i>High Fat</i>	<i>Low Fat</i>	<i>Low Fat + Omega 3</i>
Breakfast			
Wheaties	25g	35g	45g
w/ Sugar	4g	6g	6g
Orange	100g	150g	150g
w/ Sugar	0	0	5g
Orange Muffin	55g (High Fat)	50g (Low Fat)	50g (Low Fat, High Om-3)
w/ Butter/Margarine	4g (Margarine)	5g (Butter)	3g (Butter)
w/ Preserves	0	15g	0
Milk-Skim/2%	200g (2%)	200g (Skim)	240g (Skim)
Lunch:			
Chicken/Tuna Sandwich			
Whole Wheat Bread	50g	65g	65g
Lettuce/Tomato	20g/0	20g/50g	20g/50g
Cheddar Cheese	15g	0	20g
Miracle Whip-Reg/FF	10g (Reg)	15g (FF)	15g (FF)
w/ Egg Yolk	0	4g	4g
w/ Flax Oil	0	0	4g
Chicken Breast/Tuna	60g (Chicken)	70g (Chicken)	70g (Tuna)
Margarine	4g	0	0
Carrots	60g	60g	60g
Pineapple	100g	100g	100g
w/ Sugar	0	5g	5g
Dinner:			
Spaghetti with Meat Sauce			
Ragu Lite	110g	150g	150g
w/ Corn Oil	8g	0	0
Spaghetti	80g	130g	150g
Mushrooms	50g	50g	50g
Lean Ground Beef	65g	60g	40g
French Bread/White Bread	25g (White)	40g (French)	40g (French)
w/ Butter	7g	5g	0
Green Beans	100g	100g	100g
Lettuce Salad	70g	75g	75g
	20g		
w/ Italian Dressing-Reg/FF	(Reg)	15g (FF)	15g (FF)
w/ Fat Free Italian Dressing	0	15g	15g
w/ Safflower Oil/Flax Oil	0	2g (Safflower)	3g (Flax)
w/ Egg Yolk/Egg White	0	0	4.5g/15g
Peaches	90g	100g	100g
w/ Sugar	0	5g	5g
Snack			
Blondies	50g (High Fat)	50g (Low Fat)	50g (Low Fat, High Om 3)
Milk Chocolate Candy	15g	0	10g
2% Milk	180g	0	0
Gumdrops	0	35g	20g

Nutrient Composition (Calculated)

Kcal	2026	2006	2036
CHO (g/%)	230g/45%	327g/65%	323g/62%
Pro (g/%)	77g/15%	77g/15%	76g/15%
Fat (g/%)	92g/40%	46g/20%	52g/23%
Fiber (g)	21.6g	27.2g	30.5g
Chol (mg)	204.1mg	201.3mg	213mg
SFA (g)	26.9g	12.4g	14.2g
MUFA (g)	30.4g	14.7g	14.4g
PUFA (g)	27.3g	12.99	14.2g
18:3 (g)	1.21g	.577g	6.786g
20:5 (g)	.006g	.008g	0.176g
22:6 (g)	.013g	.020g	.451g
Omega 3 FA (g)	1.23g	.605g	7.413g

Sample Menu 2000 Kcal) - Day 3

	<i>Menu</i>	<i>High Fat</i>	<i>Low Fat</i>	<i>Low Fat + Omega 3</i>
Breakfast	Pineapple Juice	120g	150g	140g
	Wheat Chex	30g	30g	30g
	w/ Sugar	0	4g	4g
	WW Bread/WW Bagel	50g (Bread)	60g (Bagel)	60g (Bagel)
	w/ Cream Cheese-Reg/Lite	30g (Reg)	20g (Lite)	30g (Lite)
	w/ Diet Jelly/Preserves	10g (Diet Jelly)	20g (Preserves)	10g (Preserves)
	Milk-Skim/2%	120g (2%)	200g (Skim)	200g (Skim)
Lunch:	Chicken/Salmon Pasta Salad			
	Macaroni	80g	80g	80g
	Chicken Breast/Salmon	80g (Chicken)	55g (Chicken)	65g (Salmon)
	Green Onion	10g	10g	10g
	Diced Celery	10g	10g	10g
	Peas	15g	15g	15g
	Garlic Powder/Salt/Pepper	Dash	Dash	Dash
	Lemon Juice	2g	2g	2g
	Mayonnaise	25g	9g	0
	Fat Free Miracle Whip	0	20g	30g
	w/ Egg Yolk	0	7g	7g
	Whole Wheat Bread	25g	60g	30g
	w/ Butter/Flax Butter	10g (Butter)	4g (Butter)	5g (Flax Butter)
	Blueberries	100g	100g	100g
	w/ Sugar	0	4g	4g
	Oatmeal Walnut Cookie	30g	30g	30g
Dinner:	Beef Tenderloin	65g	60g	75g
	Mashed Potatoes	100g	140g	140g
	w/ Butter/Olive Oil	5g/4g	0	0
	Corn	80g	120g	120g
	Whole Wheat Bread	25g	30g	30g
	w/ Butter/Margarine	9g (Butter)	4g (Marg)	0
	Lettuce Salad	60g	60g	60g
	w/ Ranch Dressing-Reg/FF	15g (Reg)	15g (FF)	15g (FF)
	w/ Corn Oil/Flaxseed Oil	0	3g (Corn)	3g (Flax)
	Fruit Cocktail	90g	100g	100g
	w/ Sugar	0	4g	0
Snack	Brownie	60g (High Fat)	60g (Low Fat)	50g (LF, High Om 3)
	Raisins	0	25g	30g
<hr/>				
Nutrient Composition (Calculated)				
Kcal		2010	2011	2009
CHO				
(g/%)		232g	334g/65%	313g/61%

Pro (g/%)	75g	77g/15%	79g/15%
Fat (g/%)	92g	47g/20%	54g/24%
Fiber (g)	21.2g	27.6g	27.4g
Chol (mg)	241.3mg	218.7mg	231.8mg
SFA (g)	28.5g	13.4g	15.2g
MUFA (g)	28.6g	14.98g	16.1g
PUFA (g)	27.8g	12.8g	17.5g
18:3 (g)	1.886g	1.172g	5.073g
20:5 (g)	.008g	.006g	.449g
22:6 (g)	.016g	.019g	.955g
Omega 3 FA (g)	1.91g	1.197g	6.472g

Sample Menu 2000 Kcal) - Day 4

Menu		High Fat	Low Fat	Low Fat + Omega 3
Breakfast	Grape Juice	80g	100g	80g
	Rice Krispies	25g	30g	30g
	Whole Wheat English Muffin	40g	60g	60g
	w/ Butter/Margarine	6g (Butter)	3g (Butter)	3g (Butter)/3g (Marg)
	w/ Preserves	0	15g	15g
	Skim Milk	240g	200g	200g
Lunch:	Roast Beef Sandwich			
	White Bread	50g	50g	50g
	Roast Beef, Deli	40g	65g	65g
	Mayonnaise, Reg	22g	6g	0
	Fat Free Miracle Whip	0	10g	10g
	Flax Butter	0	0	4g
	American Cheese	30g	0	0
	Lettuce	20g	20g	20g
	Tomato	50g	50g	50g
	Fritos/Pretzels	30g (Fritos)	25g (Pretzels)	25g (Pretzels)
	Peaches	90g	100g	100g
	Blondies	0	55g (Low Fat)	55g (Low Fat)
Dinner:	Fish/Salmon Cakes	180g (Fish)	200g (LF Fish)	200g (Salmon)
	w/ Sour Cream Sauce-Reg/Lite	25g (Reg)	20g (Lite)	20g (Lite)
	w/ Dill/Salt/Pepper/Lemon	Dash	Dash	Dash
	Brown Rice	110g	120g	100g
	w/ Butter	3g	0	0
	Carrots	100g	100g	100g
	Lettuce Salad	70g	70g	70g
	w/ Egg White	25g	0	0
		15g (Low Cal)	15g (FF)	15g (FF)
	w/ French Dressing-Low Cal/FF			
	w/ Corn Oil/ Flaxseed Oil	8g (Corn)	3g (Corn)	6g (Flax)
	Whole Wheat Bread	25g	60g	60g
	w/ Butter/Flax Butter	5g (Butter)	5g (Butter)	3g (Flax Butter)
	Pears	80g	120g	120g
Snack	Skim Milk	240g	0	0
	Yoplait Lite	0	190g	150g
	Oatmeal Walnut Cookie	30g	0	0
	Dates	0	40g	40g
<hr/>				
Nutrient Composition (Calculated)				
Kcal		2003	2013	2041
CHO (g/%)		229g/45%	330g/65%	319g/62%
Pro (g/%)		73g/15%	73g/15%	73g/14%

<i>Fat (g/%)</i>	91g/40%	46g/20%	54g/24%
<i>Fiber (g)</i>	17.7g	23.6g	23.2g
<i>Chol (mg)</i>	240.96mg	196.6mg	209.6mg
<i>SFA (g)</i>	28.5g	13.4g	14.3g
<i>MUFA (g)</i>	27.97g	14.9g	17.5g
<i>PUFA (g)</i>	28.7g	13.97g	18.4g
<i>18:3 (g)</i>	2.429g	.864g	5.749g
<i>20:5 (g)</i>	.002g	.002g	.338g
<i>22:6 (g)</i>	.008g	.008g	0.72
<i>Omega 3 FA (g)</i>	2.432g	.874g	6.807g

Sample Menu 2000 Kcal) - Day 5

	Menu	High Fat	Low Fat	Low Fat + Omega 3
Breakfast	Orange Juice	120g	220g	220g
	Shredded Wheat	25g	35g	35g
	w/ Sugar	0	6g	6g
	Whole Wheat Bagel	60g	60g	60g
	w/ Cream Cheese-Reg/FF	30g (Reg)	30g (FF)	30g (FF)
	w/ Preserves	0	20g	20g
	w/ Margarine	5g	0	0
	Skim Milk	120g	200g	140g
Lunch:	Chicken/Salmon Salad Sandwich			
	Cracked Wheat Bread	50g	60g	60g
	Chicken Breast/Salmon	60g (Chicken)	45g (Chicken)	60g (Salmon)
			7g (Reg)/10g (FF)	10g (FF)
	Miracle Whip-Reg/FF	30g (Reg)		
	Egg Yolk/Flax Oil	0	7g (Yolk)	7g (Yolk)/4g (Oil)
	Lettuce Leaf	20g	20g	20g
	Carrot/Cucumber	60g/40g	60g/40g	60g/40g
	Raspberries	80g	110g	110g
	w/ Sugar	0	6g	6g
Dinner:	Brownie	50g (High Fat)	40g (Low Fat)	40g (Low Fat)
	Meatloaf	100g	80g	80g
	w/ Fat Free Gravy	40g	40g	40g
	w/ Safflower Oil/Flax Oil	7g (Safflower)	3g (Safflower)	3g (Flax)
	Mashed Potato	100g	140g	140g
	Green Beans	100g	100g	100g
	Spinach Salad	70g	70g	70g
	w/ Fat free Ranch	15g	15g	15g
	w/ Safflower Oil/Flax Oil	7g (Safflower)	4g (Safflower)	3g (Flax)
	Whole Wheat Roll	25g	45g	30g
Snack	w/ Butter	8g	0	0
	Pineapple	80g	120g	120g
	Grape Juice	0	120g	120g
	Low Fat Triscuits	25g	40g	40g
	Mozzarella Cheese	40g	25g	30g

Nutrient Composition (Calculated)

	1979	2009	2000
Kcal			
CHO (g/%)	232g/45.5%	332g/64%	320g/62%
Pro (g/%)	76g/15%	80g/15%	77g/15%
Fat (g/%)	89g/39.5%	48g/21%	54g/23%
Fiber (g)	32.7g	40.6g	39.5g
Chol (mg)	198.7mg	198.4mg	198.1mg

SFA (g)	27.3g	13.5g	14.8g
MUFA (g)	27.4g	15.7g	18.0g
PUFA (g)	27.7g	14.3g	15.8g
18:3 (g)	1.327g	.778g	5.824g
20:5 (g)	.006g	.005g	.415g
22:6 (g)	.013g	.018g	.883g
Omega 3 FA (g)	1.346g	.963g	7.122g